CARDIAC INJURY AND CARBON MONOXIDE POISONING

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Cardiac abnormalities in the presence of hypoxia have been well documented. These comprise arrhythmias and alterations in the ST segment and the T-wave of the electrocardiogram.[1] The changes are generally found over the precordial leads, but they may also be absent. When present, they take the form of slight depression of the ST segment, flattening, depression or inversion of the T-wave, premature or ectopic beats, and paroxysmal atrial fibrillation. Reduction in the voltage of the QRS complexes, prolongation of the PR interval, and intraventricular block have also been reported.[2] The basis for these changes is myocardial hypoxia which may be caused by a variety of conditions, including vasomotor syncope, severe haemorrhage, ischaemic coronary artery disease, asphyxia, toxins and drugs. As a rule, if the cause is not prolonged, and if the insult has not been profound, the electrocardiogram reverts to normal in a few days or weeks.

A less well recognized form of hypoxia which may affect the myocardium is that of poisoning by carbon monoxide. This is a colourless, odourless gas which is produced whenever incomplete combustion of carbon or carbon-containing compounds occurs. Poisoning by this gas may be accidental, suicidal or occupational. The Bantu are particularly prone to accidental poisoning during the winter months when braziers are used in their badly ventilated sleeping quarters. A well-known form of poisoning of suicidal intent is exposure to the exhausts of automobiles, while intoxication as an occupational hazard has been described in ill-ventilated boiler-rooms and among firemen, miners, and those in similar occupations.

Carbon monoxide produces its noxious effects by reducing the oxygen transport capacity of the blood. It combines with haemoglobin at the same point on the haemoglobin molecule as oxygen to form carboxyhaemoglobin. The haemoglobin oxygen dissociation curve is shifted to the left, and therefore oxygen release to the tissues is less effective.[3] The gas binds to haemoglobin with approximately 210 times as much tenacity as to oxygen, so that a carbon monoxide pressure of only 0·5 mm.Hg in the alveoli (210 times less than that of alveolar oxygen) will cause half the haemoglobin in the blood to become bound with carbon monoxide instead of with oxygen.[4] Anaemic patients will therefore suffer from carbon monoxide poisoning more severely than normal people. Many Bantu suffer from malnutrition and often anaemia, so that the effects of carbon monoxide poisoning may be expected to be clinically more severe. A carbon monoxide concentration of 0·1% is lethal.[4]

Experimental carbon monoxide poisoning of animals has resulted in petechial haemorrhages throughout the organs of the body. Vascular lesions, consisting of small haemorrhages and perivascular infiltrations are seen together with focal areas of necrosis of the heart muscle. Similar myocardial injury has been observed in humans who have succumbed to intoxication by the gas. The lesions then are confined essentially to the left ventricle. Particularly affected are the papillary muscles and endocardial region where the effect varies from areas of petechial haemorrhages to frank necrosis.[2]

Clinical evidence of myocardial involvement may appear immediately or only several days after exposure to the gas. In general, symptoms occur more acutely with high air concentrations of carbon monoxide and are most commonly referable to the central nervous system. The chief cardiac features are angina pectoris and cardiac irregularity, and atrial fibrillation has been precipitated. Palpitation, tachycardia, precordial oppression or pain, exertional dyspnoea and weakness have been noted. An attack of acute coronary occlusion has been attributed to carbon monoxide poisoning.[2]

While clinical recovery usually ensues within a day or two, the electrocardiographic abnormalities may persist and return to normal only after several weeks.[2] Few biochemical observations with these electrocardiographic abnormalities in carbon monoxide poisoning among the Bantu have been recorded. The purpose of this paper is to attempt to assess the extent of the cardiac damage on the basis of serial enzyme determinations in conjunction with changes in the electrocardiogram.

MATERIAL AND METHODS

Sixteen Bantu patients were studied. These comprised 8 cases admitted during 1964, and the last 8 cases admitted in 1963. The clinical presentations included headache, irritability, decreased exercise tolerance, confusion, collapse, stupor and coma. Transient neurological signs, including pareses and conjugate deviation of the eyes, were also noted. In a few cases the patients, on admission, were in a state of peripheral vascular collapse, and the blood pressure could only be recorded after supportive therapy had been instituted. The mucous membranes exhibited the characteristic cherry-red colour. In some cases localized pains in the chest and extremities were noted, while backache was a frequent complaint and has been observed repeatedly in this hospital.[5]

Exposure in one case occurred as an occupational hazard in a closed boiler-room (J.M.). All the other patients were affected by braziers taken into their sleeping quarters to provide warmth. Two patients, a husband and wife (S.D. and M.D.), apparently exposed to the same quantity of carbon monoxide, were admitted in different levels of consciousness. The female (M.D.) was reasonably lucid and gave an accurate history of events. The male was comatose and had probably contracted pneumonia in his unconscious state, as probably occurred also in 2 other patients (W.M. and S.S.). Such individual variation has previously been recorded. One patient (S.Nk.) was 2½-months pregnant and aborted 12 days after admission. The ages of the patients ranged from 18 to 71 years. Their blood pressures were all within normal limits, and other than the altered electrocardiographic recordings there was no evidence of any cardiovascular abnormality. There were no urinary complications and no neurological sequelae.

Examinations

The 8 patients admitted in 1964 were subjected to the following examinations:

1. An electrocardiogram was taken on admission, and at frequent intervals thereafter as was considered necessary. The minimum interval between recordings was 24 hours, and the maximum interval 7 days.

TABLE I. CONDITION ON ADMISSION AND RESULT OF INVESTIGATIONS

Patient	*Condition on admission*	*Erythrocyte sedimentation rate (Wintrobe)*	*SGOT (Normal range 2-35 units; mean 10 units)*	*SGPT (Normal range 2-35 units; mean 10 units)*	*SLDH (Normal range 100-280 units mean 170 units)*	*Radiological examination of chest*	*Electro-cardiogram*	*Other investigations*
S.L.	Comatose	2	Not estimated	Not estimated	Not estimated	No cardio-megaly	Normal	BUN 22 mg./100 ml. Blood sugar 74 mg./100 ml.
J.P.	Drowsy; found unconscious	2	Not estimated	Not estimated	Not estimated	No cardio-megaly	Abnormal	
A.B.	Conscious	1	Not estimated	Not estimated	Not estimated	No cardio-megaly	Normal	
S.Nt.	Unconscious	10	Not estimated	Not estimated	Not estimated	No cardio-megaly	Normal	
L.M.	Semicomatose; stertorous breathing	16	Not estimated	Not estimated	Not estimated	No cardio-megaly	Abnormal	
P.H.	Comatose; stertorous breathing; trismus; deviation of eyes to right; transient spasticity	20	Not estimated	Not estimated	Not estimated	No cardio-megaly	Abnormal	
S.S.	Comatose; eyes rolling; shivering; blood pressure not recordable; rigidity of limbs	36	Not estimated	Not estimated	Not estimated	No cardio-megaly; pneumonia	Abnormal	Mucoprotein 307 mg./100 ml.
W.M.	Semiconscious	6	Not estimated	Not estimated	Not estimated	No cardio-megaly; broncho-pneumonia	Normal	BUN 24 mg./100 ml. Electrolytes normal
R.B.	Confused; severe headache	1	25	25	960	Not performed	Abnormal	Carboxyhaemoglobin 22%; C. reactive protein absent; total cholesterol 196 mg./100 ml.
S.D.	Comatose; pulseless; blood pressure not recordable	35	295	57	2,000	No cardio-megaly; pneumonia	Abnormal	Carboxyhaemoglobin under 5%; C. reactive protein absent; BUN 40 mg./100 ml. Electrolytes normal; serum cholinesterase 76% of average normal activity
S.Nk.	Comatose	Not estimated	235	141	1,910	Not performed	Abnormal	Carboxyhaemoglobin under 5%
G.G.	Comatose	10	90	52	1,050	No cardio-megaly	Abnormal	Carboxyhaemoglobin 20%
M.D.	Conscious	Not estimated	160	155	1,600	No cardio-megaly	Abnormal	BUN 39 mg./100 ml. electrolytes normal
A.S.	Unconscious; later drowsy and irritable	Not estimated	35	26	500	Not performed	Abnormal	Carboxyhaemoglobin under 5%
J.M.	Severe headache	Not estimated	30	15	320	Not performed	Normal	Carboxyhaemoglobin under 5%
S.B.	Conscious	1	17	22	380	No cardio-megaly	Normal	Carboxyhaemoglobin under 5%; serum cholinesterase 100% of average normal activity

2. Estimations of serum glutamic oxalacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), and serum lactic dehydrogenase (SLDH) were made as soon as possible after admission, so that there was a minimum delay between the collection of blood and the estimation of the enzymatic components. These were repeated at weekly intervals. The normal values for these components at the laboratory where they were performed are:

SGOT range 2 - 35 units, mean 10 units
SGPT range 2 - 35 units, mean 10 units
SLDH range 100 - 280 units, mean 170 units.

3. Microscopic and chemical urine analyses were done at regular intervals.

4. In severe cases of poisoning, blood urea nitrogen (BUN), and electrolyte levels were estimated. An X-ray film of the chest was also taken, and in several patients a full haematological examination was done.

5. In some patients, estimations of carboxyhaemoglobin levels were performed, but because these samples of blood were collected several hours after treatment had been instituted, values of under 10% were usually obtained.

The results of the 1964 patients were compared with the patients admitted in 1963 when it had been the practice to perform similar routine investigations with the exception of the serum enzyme studies. The criteria for discharge in the latter cases had been:

1. The absence of tachycardia on the electrocardiogram.
2. A normal erythrocyte sedimentation rate (Wintrobe).
3. Absence of urinary and neurological complications.
4. Clinical and symptomatic well-being.

RESULTS

Ten of the 16 patients showed abnormalities in the electrocardiogram. A frequent abnormality was an inverted T-wave which was present in 3 or more of the precordial leads, usually V3 to V6 (7 cases), and most of these cases had an associated T-wave inversion in other leads as well. Flattening of the T-wave in the standard and unipolar leads occurred in one case (J.P.), and since this was associated with tachycardia, it was considered an abnormal finding. Tachycardia occurred in 8 patients, but in the majority the rate had returned to normal within 7 days. Extrasystoles were recorded in 1 patient (G.G.), but these had disappeared on discharge (10 days later). The T-waves of the electrocardiogram were normal on admission in 8 patients, but within 48 hours 2 of these patients exhibited markedly abnormal T-wave changes (G.G. and S.D.). An electrocardiogram suggestive of pericarditis developed in 1 patient 2 weeks after admission (J.M.). However, there were no other signs of pericarditis, and, since this developed 2 weeks after admission, it was not included under the abnormal electrocardiograms. There were 4 patients whose electrocardiograms were still abnormal on discharge. They and future admissions will be reviewed in a prospective study.

Radiological examination of the chest was performed in 12 cases, but no cardiac abnormality was noted, though pulmonary infection was observed in 3 patients (S.S., S.D. and W.M.). No case of pulmonary infarction was seen. The erythrocyte sedimentation rate (Wintrobe) had been performed in 12 cases, and in only 3 was the level above 16. (P.M., S.S. and S.D.). (Two of these high values were associated with pneumonia—S.S. and S.D.) Urine exami-

TABLE II. ELECTROCARDIOGRAPHIC FINDINGS

Patient	Age in years	Sex	Blood pressure	Sinus tachycardia (over 100 beats/min.)	ST segment	T-wave	Other changes	Comment
S.L.	29	M	105/70	No	Normal	Diphasic V1+V2	Nil	Normal electrocardiogram
J.P.	38	M	110/80	Yes	Depressed in standard leads	Flattened in standard and unipolar leads	Nil	Tachycardia absent on discharge, with normal ST segments and T-waves
A.B.	27	M	120/85	No	Normal	Inverted in V1+V2	Nil	Normal electrocardiogram
S.Nt.	18	F	120/80	No	Normal	Inverted in standard III, AVR and V1. Diphasic in V2	Nil	Probably a normal electrocardiogram
L.M.	23	F	104/86	No	Normal	Inverted in standard I, II, III, AVL, and V2–V6	Nil	Precordial T-wave abnormalities still evident on discharge, but less marked
P.H.	35	F	112/70	Yes	Normal	Normal	Nil	Tachycardia absent on discharge
S.S.	29	F	114/80	Yes	Depressed in standard II	Inverted in standard I, II, III, AVF, and V3–V6	Nil	Precordial T-wave abnormalities still present on discharge one month later
W.M.	50	M	145/90	No	Normal	Normal	Nil	Normal electrocardiogram
R.B.	30	M	110/85	No	Normal	Inverted in V1–V6	Upright U-wave in V2 and V3	On discharge 3 weeks later T-waves diphasic in V1 and V2, and inverted V3–V6
S.D.	46	M	135/85	Yes	Normal	Normal on admission. Inverted in V1–V6, 2 days later	Nil	T-waves still inverted V1–V6 on discharge 4 weeks later, but less marked
S.Nk.	46	F	110/80	Yes	Normal	Inverted in V3–V6	Nil	T-waves normal and no tachycardia on discharge 3½ weeks later
G.G.	35	F	105/85	Yes	Normal	Normal on admission and inverted V1–V4 2 days later	Extrasystoles	Extrasystoles disappeared on discharge, and T-waves returned to normal
M.D.	49	F	120/80	Yes	Normal	Inverted in standard I, II, III, AVL, AVF, and V2–V6	Peaked P-waves in standard II	Normal electrocardiogram on discharge 1½ weeks later
A.S.	40	M	100/80	Yes	Raised in V2 and V3	No abnormality	Nil	Tachycardia settled by end of first week. ST segments normal
J.M.	29	M	130/80	No	Normal on admission, but elevated in standard I with reciprocal inversion standard III 2 weeks after admission	No abnormality	Nil	ST segment abnormality simulated that of pericarditis but no other signs of pericarditis
S.B.	33	M	105/85	No	Normal	Normal	Nil	Normal electrocardiogram

nation was completely normal in all patients, and, where performed, the BUN and electrolyte levels were also normal. There was no jaundice and no clinical evidence of hepatic dysfunction. There was also no muscle wasting and no haemolysis. However, evidence of tissue damage was displayed by the abnormally high levels of the serum enzymes. The SLDH was elevated in all the patients and the SGOT and SGPT only in the very severe cases. The high levels were associated with abnormal electrocardiograms in all but 1 patient (J.M.), where the levels are possibly at the upper range of normality. The highest levels of SLDH were found in the patient who aborted (S.Nk.) and in the patient suffering from pneumonia (S.D.). Here the level was still elevated 1 week after radiological resolution of the pneumonia. The average period for the return to normal levels of the SGOT and SGPT was 1 week, and for the SLDH 3½ weeks, the latter coinciding with the average duration of hospitalization. Clinical recovery occurred in all cases by the end of the first week, and in most cases within 72 hours.

Treatment was conventional, and all patients were given 5 - 7 litres of oxygen/min. administered through a face mask. Supportive therapy was instituted where indicated, and no antibiotics were used except in the presence of infection.

DISCUSSION

The transaminases and lactic dehydrogenases are essentially intracellular enzymes concerned in the metabolism of proteins and carbohydrates. The activity of most of these enzymes in the serum is low, though possibly all could be detected by sufficiently sensitive methods. Any damage to a cell which causes an increase in the permeability of the cell membrane, even without actual necrosis, will allow escape of its intracellular contents into the extracellular fluid. Damage to a cell may occur from a mechanical, electrical, chemical or hypoxic stimulus, the common denominator in all probably being hypoxia, with resultant interference in cellular respiration and the integrity of the cell membrane. During carbon monoxide poisoning less oxygen is available for tissue metabolism, and hypoxic damage occurs with consequent increase in serum enzyme activity. The latter reflects cell destruction, whether it be partial or complete. Since the intracellular enzymes have a wide distribution in the body, and as the damage is probably generalized, an elevation of the serum transaminases and serum lactic dehydrogenases may be expected. These enzymes do not necessarily change in proportion to the concentrations in the damaged tissues. The enzyme levels may also be affected by altered rates of excretion by, or damage to, the hepato-biliary or renal tract and other factors.[6] In all the cases, however, there was no obvious evidence of associated hepatic or renal dysfunction, either before or subsequent to carbon monoxide exposure.

Elevation of the SGOT and SGPT is found particularly with destruction of any tissue rich in these enzymes, not-

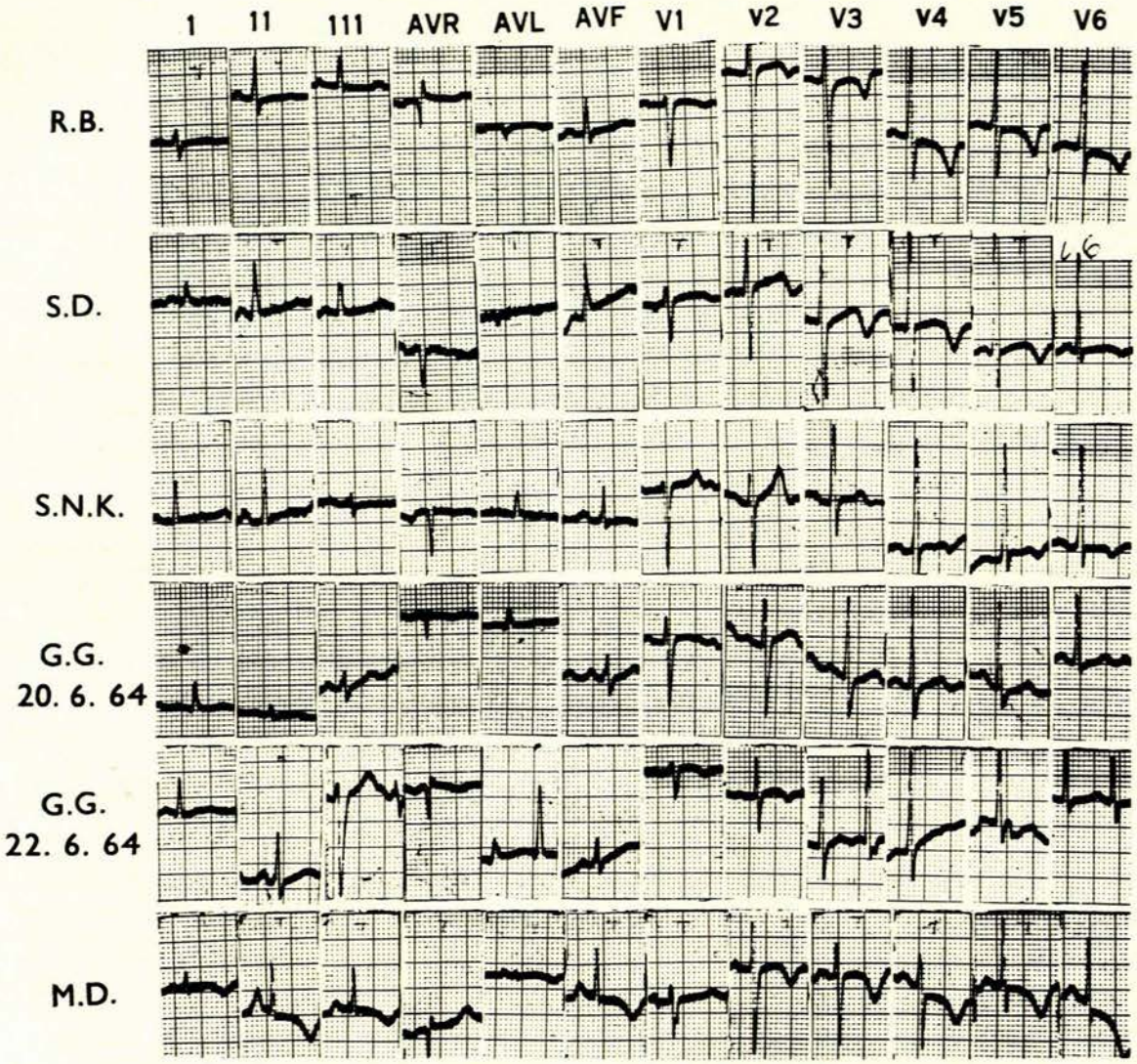

Fig. 1. Electrocardiograms after admission. Serum enzymes elevated.

ably the myocardium. A large quantity of the enzymes is also present in the liver, and moderate quantities in skeletal muscle, the kidney and the pancreas. While it is possible that part of the high titres of the enzymes may have been derived from these tissues, associated features of any damage to them were entirely absent. The brain also has a relatively high content of SGOT, but, unless there is a severe neurological catastrophe, very little, if any, of the enzyme escapes into the circulation. Since there was no haemolysis, the small quantity of SGOT present in the erythrocytes cannot account for these findings.[6]

The enzyme lactic dehydrogenase catalyses the interconversion of lactate and pyruvate, and has a wide tissue distribution. It is particularly abundant in the myocardium, kidney, skeletal muscle, liver and erythrocytes, and its activity, in both serum and tissues, is due to 5 components. These isoenzymes have recently been separated out, but this division is as yet not part of the routine procedure in our laboratory. Consequently only assay of the heterogeneous group as an entity could be made. After myocardial infarction a diagnostic titre of SLDH may not be found until after 24 hours; the maximum value is reached 48 - 72 hours later, and the level may return to normal over a period of 6 - 14 days.[6] In carbon monoxide poisoning elevated levels were found within 24 hours, and often within the range of the diagnostic titre for cardiac injury. These were the highest titres recorded, since blood samples were only collected on admission and at weekly intervals, and a return towards normal levels was evident by the end of the first week. The normal range was reached in 3 - 4 weeks. Elevation of the SLDH level up to 500 units has been observed in patients with pneumonia in this hospital,[7] and this may account for part of the high titre seen in the patient with the associated pulmonary infection. A similar explanation may be valid for the patient who aborted.[7]

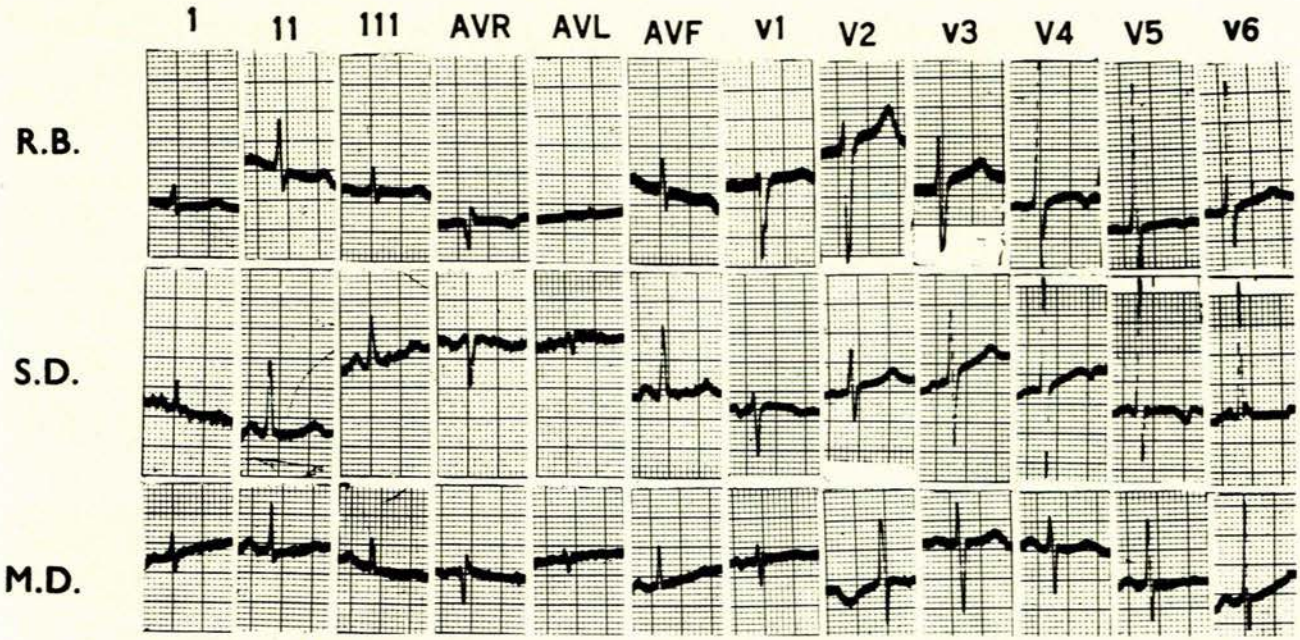

Fig. 2. Electrocardiograms on discharge. Serum enzymes normal.

Although significant amounts of SLDH are present in the liver and erythrocytes, and lesser quantities in the kidney and skeletal muscle, these tissues, as stated above, were clinically unaffected.

Myocardial injury of variable degree was reflected by abnormalities in the electrocardiograms, despite the presence of a normal erythrocyte sedimentation rate in most patients. There was, however, in this study, a close correlation between the elevated serum enzyme titres (especially SLDH) and the abnormal electrocardiograms, as has previously been observed in this hospital.[5] In some cases the electrocardiographic abnormalities persisted, despite the return to normal of the serum enzymes. Since the electrocardiogram may be normal on admission, and since some patients may not exhibit any abnormality in the electrocardiogram (as shown in half of the cases studied in 1963), it is suggested that the transaminases and SLDH, serially determined, be taken as an important parameter of prognosis. Also, in obscure cases, and lacking a definite history of exposure, the SLDH may possibly have some confirmatory diagnostic value.

SUMMARY

Sixteen cases of carbon monoxide poisoning in Africans are recorded. The pathology of the condition is described and the pathophysiology is reviewed. The presence of electrocardiographic abnormalities in carbon monoxide poisoning is discussed. Attention is drawn to the abnormalities of the serum enzymes in association with the myocardial injury found in this condition.

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REFERENCES

1. Wood, P. (1956): *Diseases of the Heart and Circulation*, pp. 109 - 111. London: Eyre and Spottiswoode.
2. Friedberg, C. K. (1956): *Diseases of the Heart*, pp. 1053 - 1056. London: Saunders.
3. Eastham, R. D. (1963): *Biochemical Values in Clinical Medicine*, p. 29. Bristol: Wright.
4. Guyton, A. C. (1961): *Textbook of Medical Physiology*, p. 549. London: Saunders.
5. Meyer, J. (1964): Personal communication.
6. Baron, D. N. and Dawson, A. M., eds. (1964): *Recent Advances in Medicine*, 14th ed., pp. 77 - 86. London: Churchill.
7. Jaffe, N. (1964): Unpublished data.